510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE

A. 510(k) Number:

k121823

B. Purpose for Submission:

New device

C. Measurand:

Sweat chloride

D. Type of Test:

Quantitative coulometric titration chloride

E. Applicant:

Wescor, Inc.

F. Proprietary and Established Names:

ChloroChek Chloridometer

ChloroChek Reagent Set

Wescor Sweat Controls (Levels 1, 2, 3)

100 mmoL/L NaCl/H2O Standard Solution

G. Regulatory Information:

1. Regulation section:

Regulation	Name	Classification	Product Code	Panel
21 § 862.1170	Chloride test system	II	JFS	(75) Chemistry
21 § 862.1660	Quality Control	I, reserved	JJX	(75) Chemistry

H. Intended Use:

1. Intended use(s):

   See indications for use below.

2. Indication(s) for use:
   The Wescor ChloroChek Chloridometer test system is intended for the quantitative in vitro diagnostic determination of chloride in human sweat using the principle of coulometric titration. Sweat chloride measurements are used in the diagnosis of Cystic Fibrosis. It is for use in Clinical Laboratory settings. The Wescor ChloroChek Chloridometer test system consists of the ChloroChek Chloridometer and the ChloroChek Reagent Set.

   The ChloroChek Reagent Set (SS-248), is to be used on the ChloroChek. It is used as the titration matrix during the titration process.

   The 100 mmoL/L NaCl/H2O Standard Solution (SS-251), is to be used on the ChloroChek. It is used as a calibration verifier, and quality control solution.

   The Wescor Sweat Controls (SS-150), levels #1, #2, and #3, are to be used on the ChloroChek. They are used as quality control solutions.

3. Special conditions for use statement(s):

   In vitro diagnostic use only.

   Prescription use only.

4. Special instrument requirements:

   ChloroChek Chloridometer

I. Device Description:

The ChloroChek Chloridometer sweat chloride analyzer is an automated device that measures chloride concentration using the principle of coulometric titration. The analyzer uses system reagents for *in vitro* diagnostic measurements of chloride in sweat samples. The ChloroChek Chloridometer sweat chloride analyzer is designed as a table-top system with all components contained in one unit. The primary components of the ChloroChek Chloridometer sweat chloride analyzer are the anode-silver electrode, cathode-silver electrode, measurement electrode, titration beaker, magnetic stir bar, magnetic stir bar retriever, silver cleaning cloth with oxidation protection, and the associated solutions contained in the ChloroChek Reagent Kit (acid buffer solution and stabilizer-gelatin solution), the conditioning solution of 10 x 0.75 mL, 100 mmol/L ampules of NaCl.

The ChloroChek Reagent Set, Conditioning Solution, and Wescor Sweat Control Solutions are provided with the device in the installation kit but need to be reordered separately for subsequent use.

The Wescor Sweat Controls are provided as 3 levels of ready to use ampules of control material. Each ampule contains an aqueous electrolyte solution, preservatives and sodium azide..

The 100 mmol/L $NaCl/H_2O$ Standard Solution is a sodium chloride solution used as a calibration verifier quality control solution..

J. Substantial Equivalence Information:

1. Predicate device name(s):

Predicate device name	510(k) number
Buchler Chloridometer Acid Reagent	k760394
Sweat Control for Cystic Fibrosis	k943925
100 mmol/L $NaCl/H_2O$ Standard Solution	k791312

3. Comparison with predicate:

ChloroChek Chloridometer

Similarities		
Item	Proposed device	Predicate device (k760394)
Intended Use	Same	In vitro measurement of Chloride
Measurement Principle	Same	Coulometric titration with amperometric indication of endpoint
Resolution	Same	1 mEq/L over a 20 second measurement duration
Reagents	Same	Liquid, ready-to-use
Measuring Range	Same	10 mmol/L to 160 mmol/L
Limitations	Same	Halogens (iodine, bromide, etc.) interfere, if present
Reference Range	Same	Sweat chloride: Infant (0-6 months): *Normal range ≤ 29 mmol/L* *Intermediate range 30-59 mmol/L* *Indicative of CF range ≥ 60 mmol/L* 6 months to >18 yrs: *Normal range ≤ 39 mmol/L* *Intermediate range 40-59 mmol/L* *Indicative of CF range ≥ 60 mmol/L*

Differences		
Item	Proposed device	Predicate device (k760394)
Sample Type	Human sweat	Human sweat, serum, plasma, urine
Sample size	10 mcL	10 mcL on LOW range setting, 100 mcL on HIGH range setting
Working Reagent Stability	Replaced with each test	Stable for eight hours at room temperature
Calibration Frequency	Factory calibrated	Factory calibrated. Users can adjust if error exceeds specifications

Wescor Sweat Controls

Similarities		
Item	Proposed device	Predicate device (k943925)
Intended Use	Same	Quality control for chloride measurement
Number of control levels	Same	Low, Medium, High

100 mmoL/L NaCl/H_2O Standard Solution

Similarities		
Item	Proposed device	Predicate device (k791312)
Intended Use	Same	Aqueous based 100 mmol/L chloride standard for use with digital and direct reading chloridometers

K. Standard/Guidance Document Referenced (if applicable):

CLSI EP5-A2: Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline—Second Edition.

CLSI C34-A3: Sweat Testing: Sample Collection and Quantitative Chloride Analysis; Approved Guideline—Third Edition.

CLSI EP6-A: Evaluation of the Linearity of Quantitative Measurement Procedure: A Statistical Approach; Approved Guideline.

CLSI EP17-A: Protocols for Determination of Limits of Detection and Limits of Quantification—Approved Guideline.

CLSI EP9-A2: Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline—Second Edition.

IEC 61010-1, Safety Requirements for Electrical Equipment for Measurement, Control, and Laboratory Use.

EN 61326-2-9-6, Electrical Equipment for Measurement, Control, and Laboratory Use—EMC requirements, Parts 2-6.

FDA Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices; May 11, 2005

FDA Guidance for Off-the-Shelf Software Use in Medical Devices; June 4, 1997.

L. Test Principle:

The ChloroChek Chloridometer sweat chloride analyzer operates according to the principle of coulometeric titration. Two silver electrodes (anode and cathode), are dipped into a measuring vessel filled with working solution consisting of an acid buffer and a colloid stabilizer. A constant current (generator current) flows between the anode and cathode. The acid buffer provides hydrogen ion (H+) which is reduced to H_2 at the cathode. A generator current flows between the anode and cathode at a constant rate thereby releasing a constant number of silver ions (Ag+) from the anode. Any chloride (Cl-) from the sample dissociates and binds to the free silver ions in solution forming silver chloride (AgCl) which is kept in solution with the colloid stabilizer. The measuring electrode senses the change in potential when excess Ag+ are present due to the exhaustion of available Cl- from the sample. The results are a direct readout of the titrated Cl- ions.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Using CLSI EP5A2, repeatability was performed using 1 ChloroChek Chloridometer sweat chloride analyzer and 1 reagent lot.

Within run precision was obtained by performing 2 runs per day, two measurements per run for 1 standard (100 mmol/L) and 3 concentrations of control materials (Low, Medium, and High), using one ChloroChek analyzer and one reagent lot (n=80) for 20 days. The results were:

Sample	Mean(mmol/L)	SD	%CV
Low Sweat Control	23.0	0.55	2.4%
Medium Sweat Control	49.7	0.72	1.4%
High Sweat Control	98.9	0.82	0.8%

Total precision study was performed using 2 ChloroChek analyzers, 2 reagent lots and 3 operators. 3 levels of control materials, and 2 Standard Solutions were

analyzed covering the measuring range of the device. Controls were analyzed in duplicate twice per day for consecutive 10 days (n=240). Summarized results are below:

	Instrument 1			Instrument 2			Overall		
Sample	**Mean mmol/L**	**SD**	**%CV**	**Mean mmol/L**	**SD**	**%CV**	**Mean mmol/L**	**SD**	**%CV**
Low Sweat Control	22	0.9	4.0	22	0.9	4.1	22	0.9	4.0
Medium Sweat Control	49	0.8	1.5	49	0.9	1.9	49	0.8	1.7
High Sweat Control	98	0.9	0.9	98	0.9	1.0	98	1.0	1.0
100 mmol/L NaCl Standard	100	1.0	1.0	100	1.0	1.0	100	1.0	1.0
10 mmoL/L NaCl Standard	10	0.6	5.6	10	0.6	5.5	10	0.6	5.6

b. Linearity/assay reportable range:

The linearity study was based on CLSI EP6-A. 11 samples covering the measuring range of the ChloroChek test system were formulated using NIST traceable NaCl (SRM 2201) and analyzed in triplicate on 1 instrument with one reagent lot. Results were analyzed using 1st, 2nd, and 3rd order least-squared regression to obtain the linear and non-linear regression coefficients. Results were as follows:

Dilution	**Mean**	**Expected values mmol/L**	**Difference Observed - Expected**
0%	8.4	8.4	0.0
10%	24.3	24.0	0.3
20%	39.9	39.6	0.4
30%	55.2	55.2	0.0
40%	71.7	70.8	0.8
50%	87.4	86.5	0.9
60%	103.0	102.1	1.0
70%	117.9	117.7	0.3
80%	134.4	133.3	1.1
90%	148.9	148.9	0.0
100%	166.5	164.5	2.0

$$y = 0.9933x - 0.0407, R^2 = 0.9999$$

The linearity study supports the sponsor's claimed measuring range of 10-160 mmol/L for the Chlorocheck test system and meets the recommended measuring range for sweat chloride analysis by the National Cystic Fibrosis Foundation, and

CLSI EPC34-A3. .

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

The ChloroChek Chloridometer is factory calibrated. Calibration is verified using the 100 mmol/L NaCI/H2O Standard Solution.

The 100 mmol/L NaCI/H2O Standard Solution and is purchased from a commercially available source. The value is gravimetrically assigned and verified on the Wescor ChloroChek. Stability and storage protocols were reviewed and found to be acceptable. Conditions were evaluated and verified for the following temperature and time limits: open vial stability 23-34°C for 30 minutes, closed vial stability 5-45°C for 60 months.

The Wescor Sweat Controls consist of Low, Medium and High chloride concentrations and are purchased from a commercially available source. Value assignment of the controls for the ChloroChek Chloridometer is performed by averaging multiple replicates on one instrument and multiplying the means by ± 0.10 to determine the expected assigned ranges for each control level. Stability and storage conditions protocols were reviewed and found to be acceptable. The sponsor claims open vial stability 23-34°C for 60 minutes and closed vial stability 25°C until expiration date in labeling.

Shelf life stability for the ChloroChek Reagent protocols were reviewed and found to be acceptable. Conditions were evaluated and verified for the following temperature and time limits: stability for 3 years after manufacturing when stored at 5-45°C.

d. Detection limit:

Limit of the Blank (LoB) and Limit of Detection (LoD) studies were based on CLSI EP17-A2. Distilled water was used as a blank solution and analyzed 60 times. Mean, median and SD were calculated.

$$\text{LoB} = 0 \text{ mmol/L}$$

LoD studies were performed using 4 diluted sample pools prepared from 4 different Sweat Control lots in order to obtain a concentration close to four times the calculated value of the LoB. The data were not Gaussian, therefore, the sponsor calculated the LoD with the formula $\text{LoD} = \text{LoB} + D_{s\beta}$ where $D_{s\beta}$ is determined by calculating the median minus the 5^{th} percentile of low concentration of the sample distribution.

$$\text{LoD} = 0.0 + [(4.6 + 4.7)/2] = 4.65 \text{ mmol/L}$$

e. Analytical specificity:

CLSI C34-A3, Sweat Testing: Sample Collection and Quantitative Chloride Analysis; Approved Guideline—Third Edition was referenced for specificity information for the ChloroChek based on the technology used by this device. CLSI states in section 9.6 that "In addition to chloride, other halides such as bromide and iodide are also detected using a chloridometer. Therefore, if a sweat sample contains other halides in addition to chloride, they will be detected and can falsely elevate the sweat chloride result."

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

Sweat samples were collected from 2 locations using an FDA cleared sweat collection device (k853973) from 80 individuals. The ages of the participants ranged from 17 months to 67 years old. The natural samples ranged from ≤ 10 to 100 mmol/L. In order to cover the measuring range, 9 spiked samples were added (n=89) to cover the high end of the range (131-160). Singlicate results from the ChloroChek test system were compared to the calculated mean of duplicate analyses for each sample on the predicate. Linear regression was calculated with results shown below:

Slope (95% CI)	Intercept (95% CI)	R^2
0.9999 (0.976, 1.022)	0.875 (-0.659, 2.410)	0.9886

Classification of samples as negative, intermediate, and indicative of Cystic Fibrosis (CF) were made following the labeled instructions for expected ranges for sweat chloride.

Comparison to the predicate is as follows:

		Predicate			**Total**
		+*	**±****	**-*****	
ChloroChek	+	21	0	0	21
	±	0	6	0	6
	-	0	0	53	53
	Total	21	6	53	80

*+ = positive, **± = indeterminate, -*** = negative

Positive percent agreement=100%, Negative percent agreement=100%, Intermediate percent agreement=100%, Overall percent agreement = 100%

An additional study was performed at a third location on 90 sweat samples. Samples were collected using an FDA cleared sweat collection device (k853973) and analyzed in singlicate on both the new device and the predicate using labeled instructions. The study participants ranged in age from 0.5 months old to 63 years old and sweat chloride concentrations ranged from ≤ 10 to 120 mmol/L. The results were:

Slope (95% CI)	Intercept (95% CI)	R^2
1.066 (1.043, 1.089)	-0.979 (-1.876, -0.082)	0.9896

Classification of samples as negative, intermediate and indicative of Cystic Fibrosis (CF) were made following the labeled instructions for expected values for sweat chloride.

Comparison to the predicate is as follows:

		Predicate			**Total**
		+	±	-	
ChloroChek	+	8	0	0	8
	±	0	3	1*	4
	-	0	0	78	78
	Total	8	3	79	90

* The result on the predicate device was 38 mmoL/L and was 41 mmoL/L on the new device. This sample was from an individual older than 6 months old and was borderline for the intermediate category (40-59 mmoL/L). CLSI C34-A3 recommends repeating intermediate results.

Positive percent agreement=100%, Negative percent agreement=98.7%, Intermediate percent agreement=75%, Overall percent agreement = 98.8%

b. Matrix comparison:

Not applicable.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off**:**

   Not applicable

5. Expected values/Reference range[1]:

Age	Normal Range	Intermediate Range	Indicative of CF Range
Infants (0-6 months)	Cl- ≤ 29 mmol/L	Cl- 30-59 mmol/L	Cl- ≥ 60 mmol/L
Beyond infancy (6 months to 18 yrs)	Cl- ≤ 39 mmol/L	Cl- 40-59 mmol/L	Cl- ≥ 60 mmol/L
Adults (> 18 yrs)	Cl- ≤ 39 mmol/L	Cl- 40-59 mmol/L	Cl- ≥ 60 mmol/L

[1]CLSI C34-A3: Sweat Testing: Sample Collection and Quantitative Chloride Analysis; Approved Guideline—Third Edition.

N. Instrument Name:

Wescor ChloroChek Chloridometer

O. System Descriptions:

1. Modes of Operation:

   Single sample testing mode

2. Software:

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes __X___ or No _____

3. Specimen Identification:

   Manual entry of sample identification is accomplished via a touch screen.

4. Specimen Sampling and Handling:

   Individual samples are pipetted into the working reagent. The device begins titrating immediately. When the device stops titrating, the result is displayed

5. Calibration:

   The Wescor ChloroChek is factory calibrated.

6. Quality Control:

Three levels of quality control material are sold separately. Recommendations in the labeling explain the frequency of quality control measurements and the assigned ranges for the ChloroChek are included in the control labeling.

The 100 mmol/L NaCI/H2O Standard Solution verifies calibration and can be used as a high control. Labeling recommends calibration verification intervals.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.